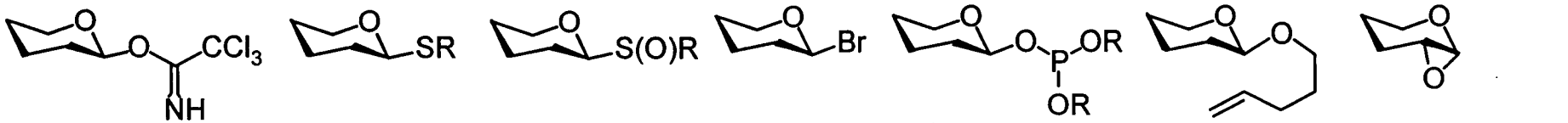
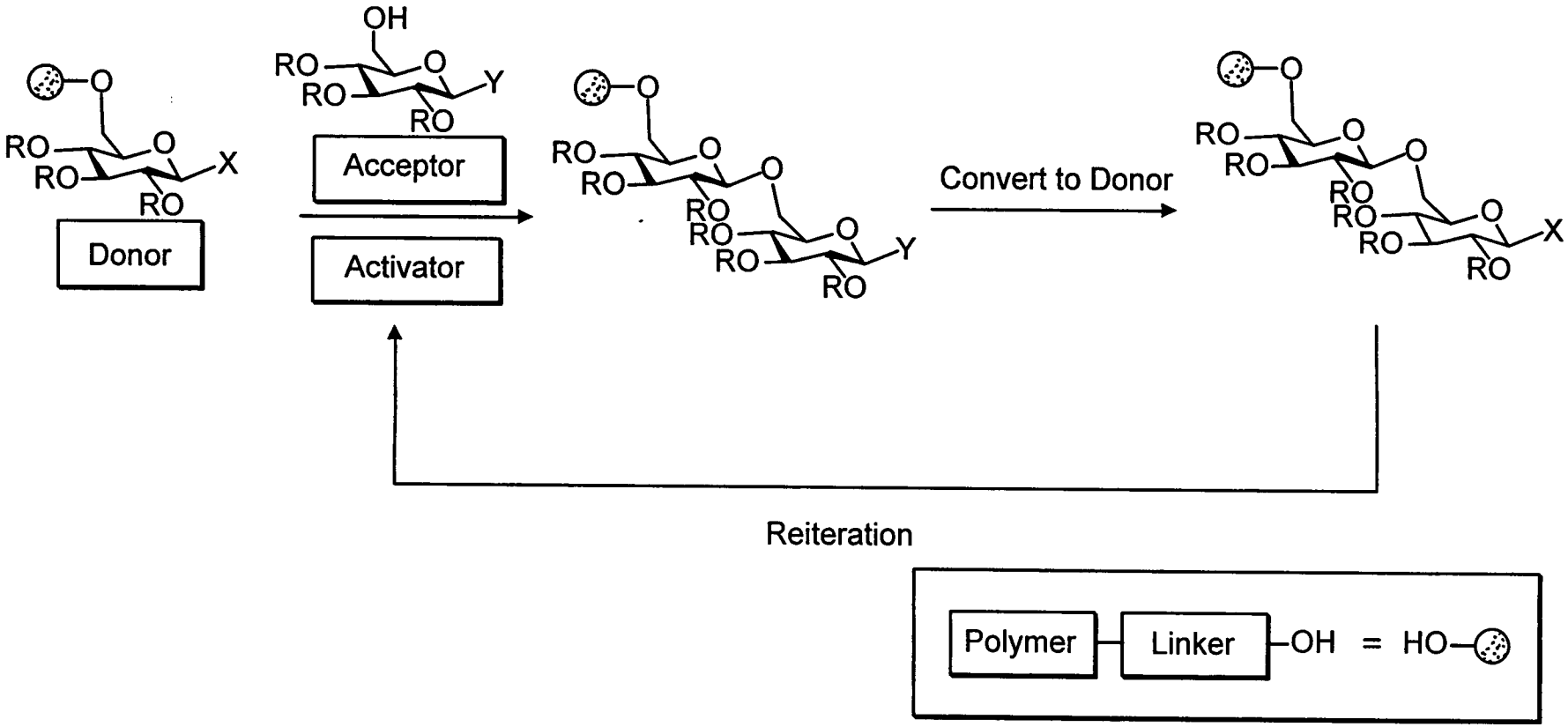


Glycosyl Trichloroacetimidate | Thioglycoside | Glycosyl Sulfoxide | Glycosyl Halide | Glycosyl Phosphite | Pentenyl Glycoside | 1,2-Anhydrosugar

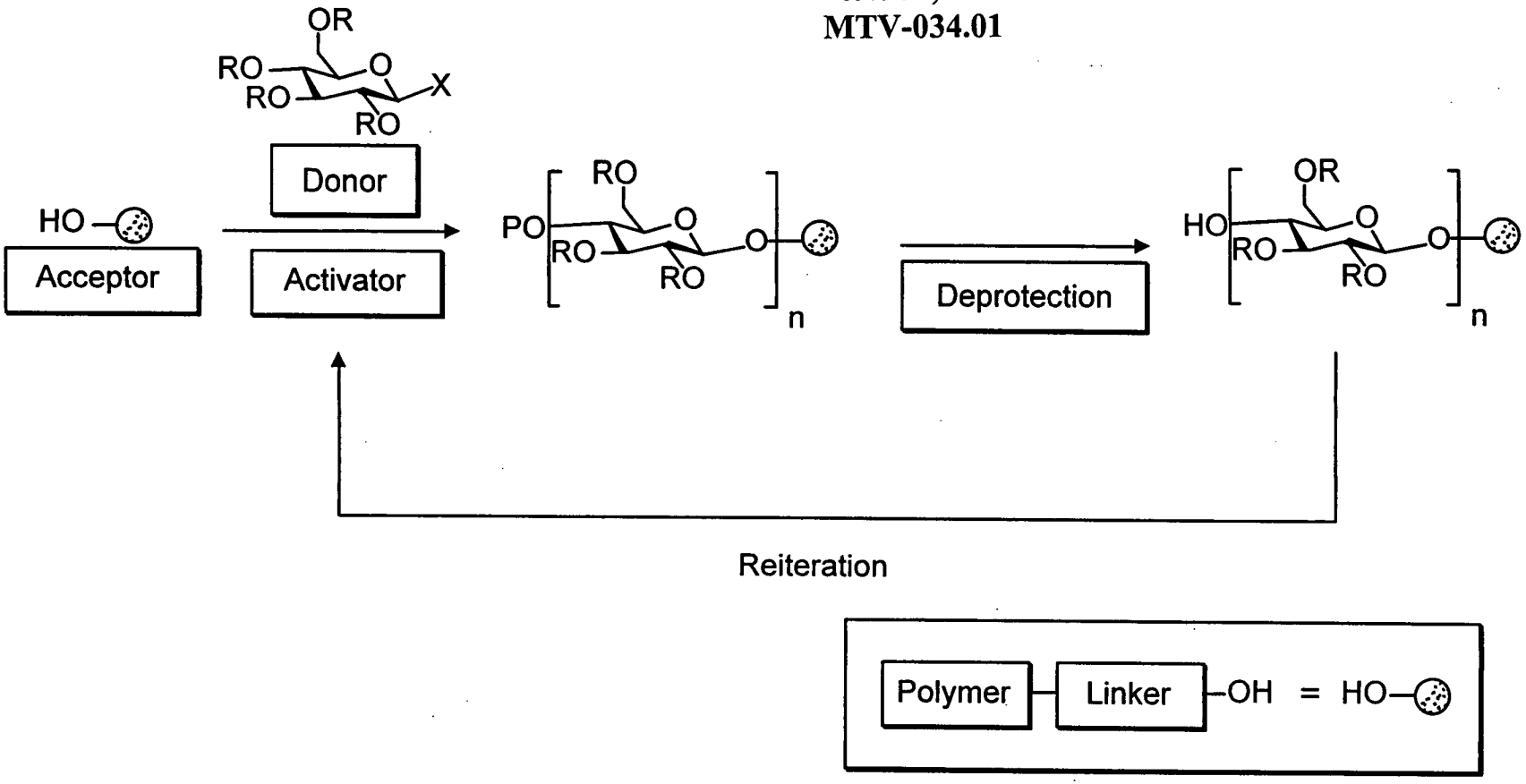
Commonly used glycosylating agents

FIG. 1



Donor bound solid-phase carbohydrate synthesis

FIG. 2



Acceptor bound solid-phase carbohydrate synthesis

FIG. 3

oligonucleotides

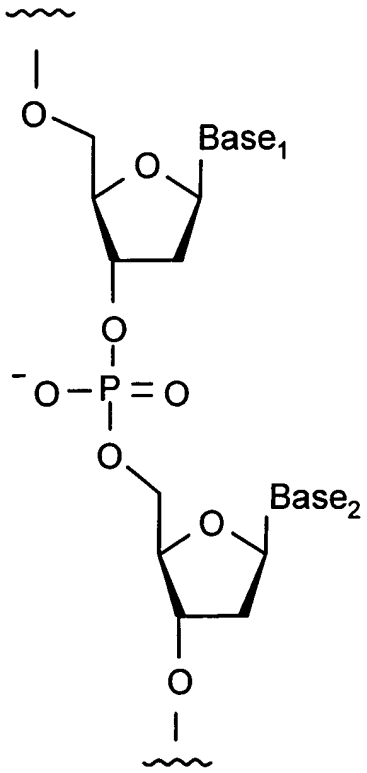


FIG. 4A

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oligopeptides

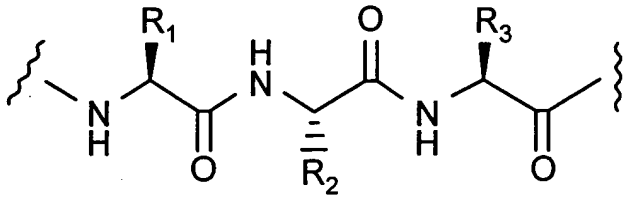

FIG. 4B

oligosaccharides

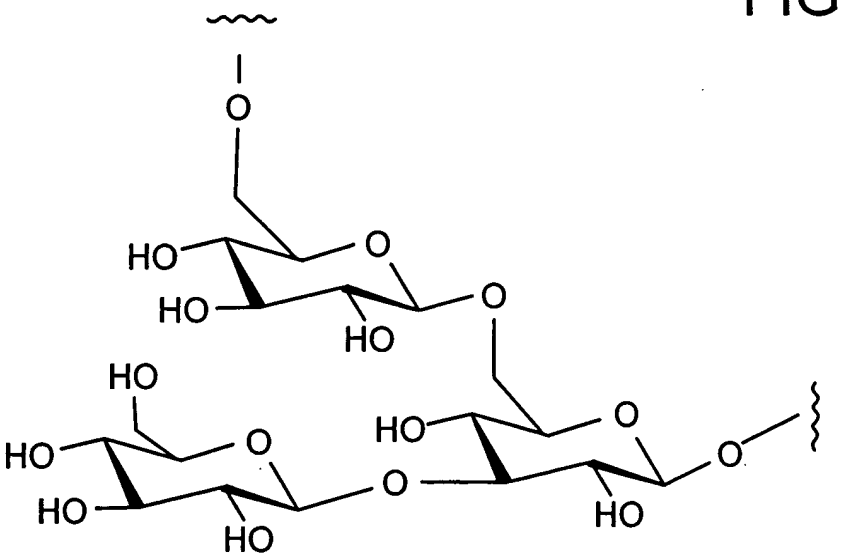

FIG. 4C

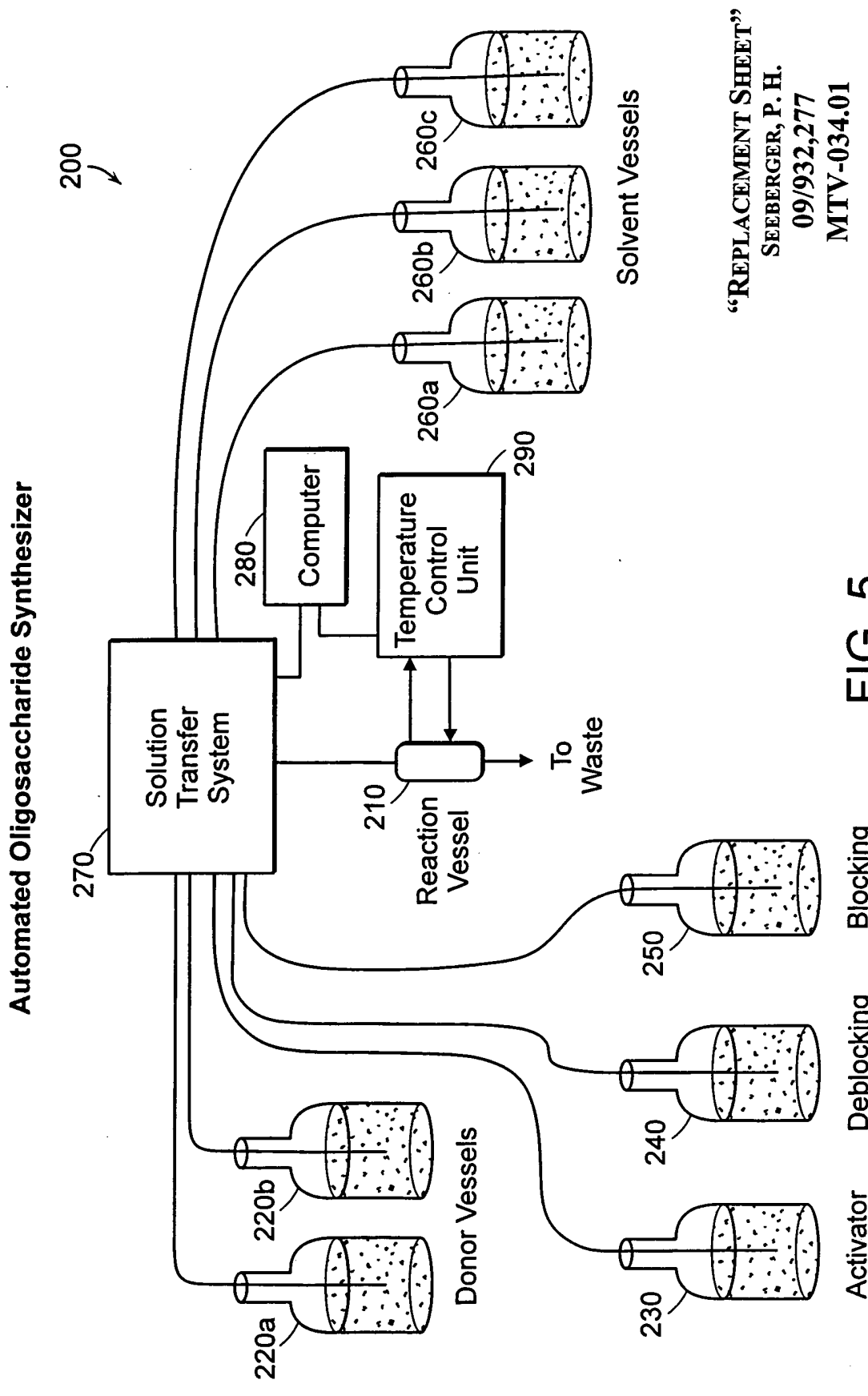

FIG. 5

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Automated Oligosaccharide Synthesizer

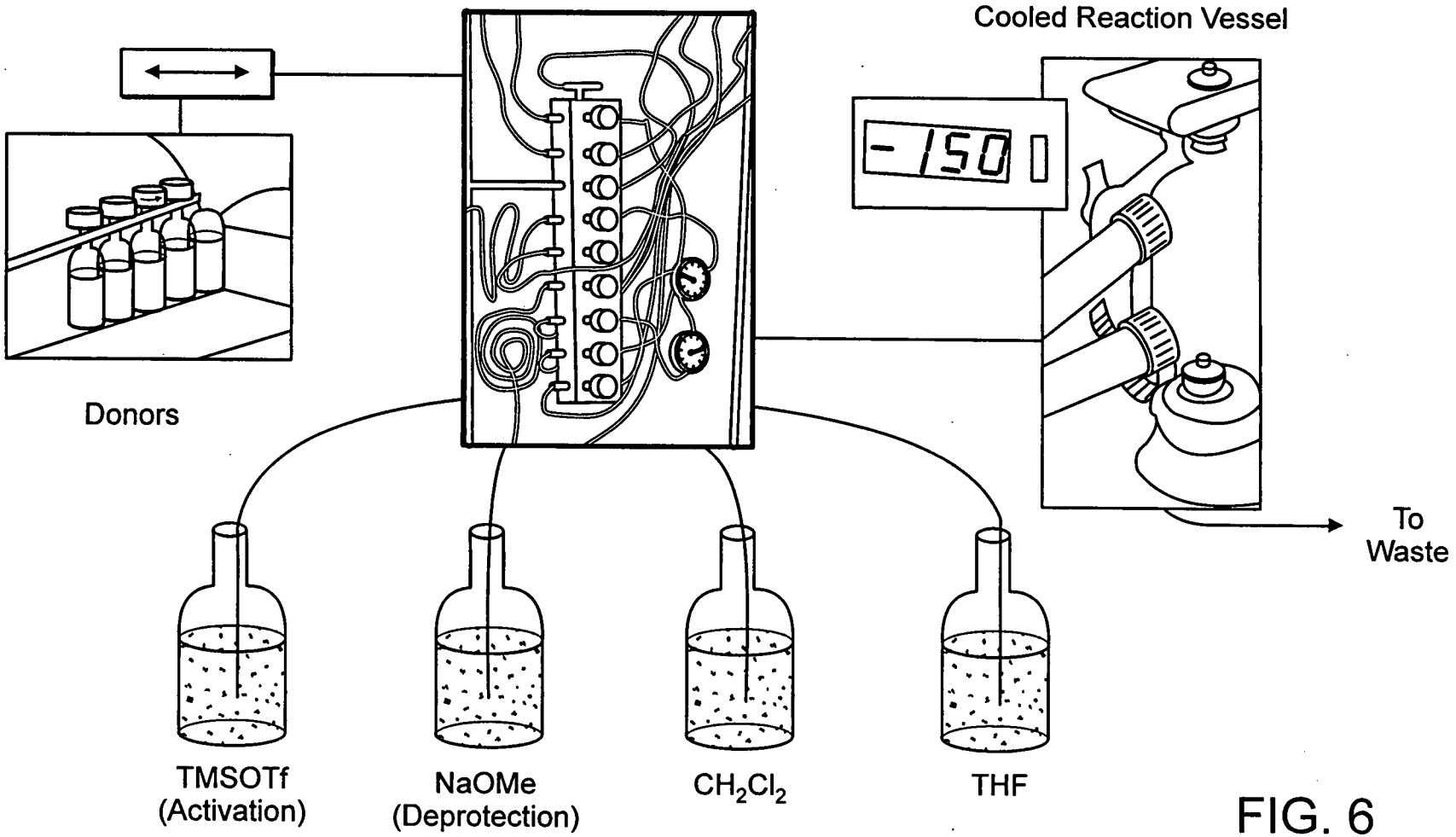

FIG. 6

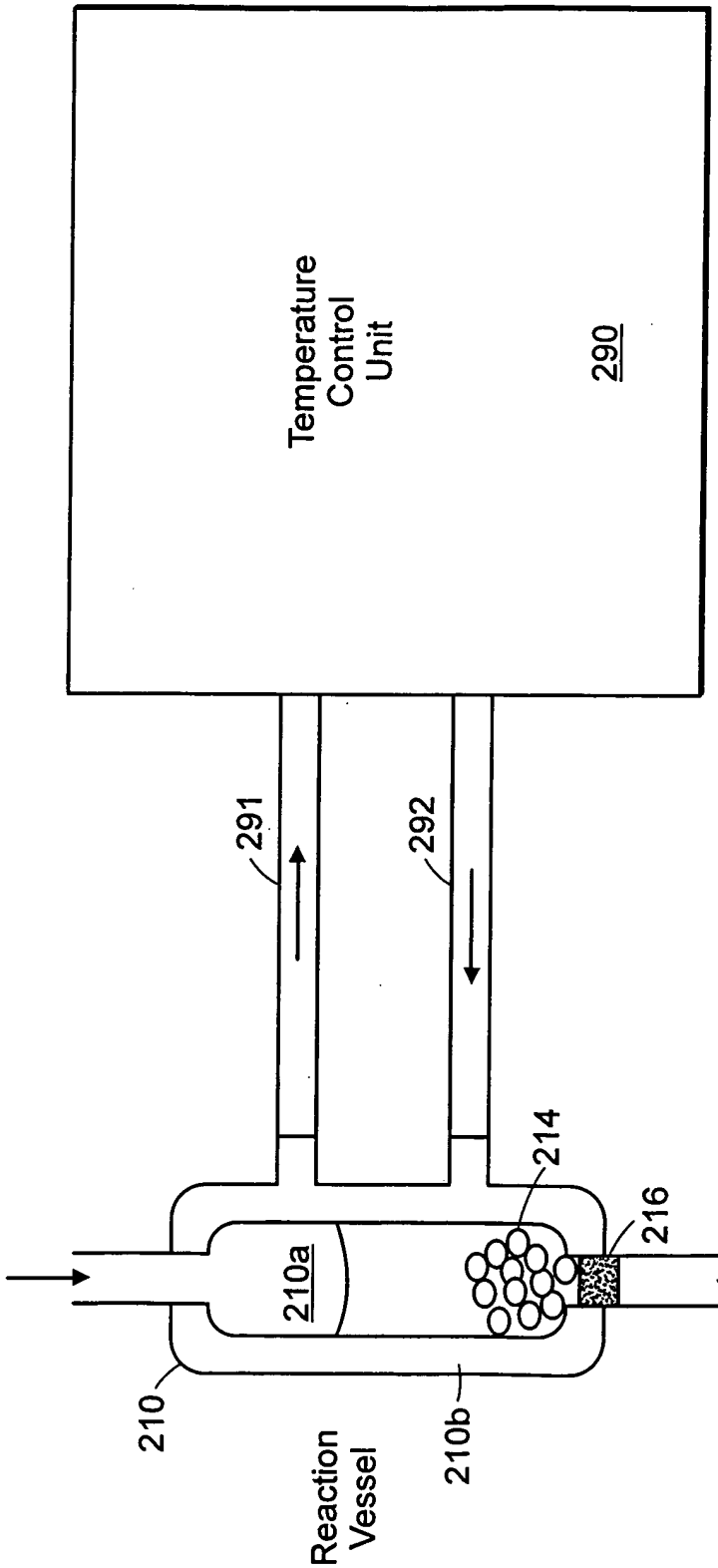

FIG. 7

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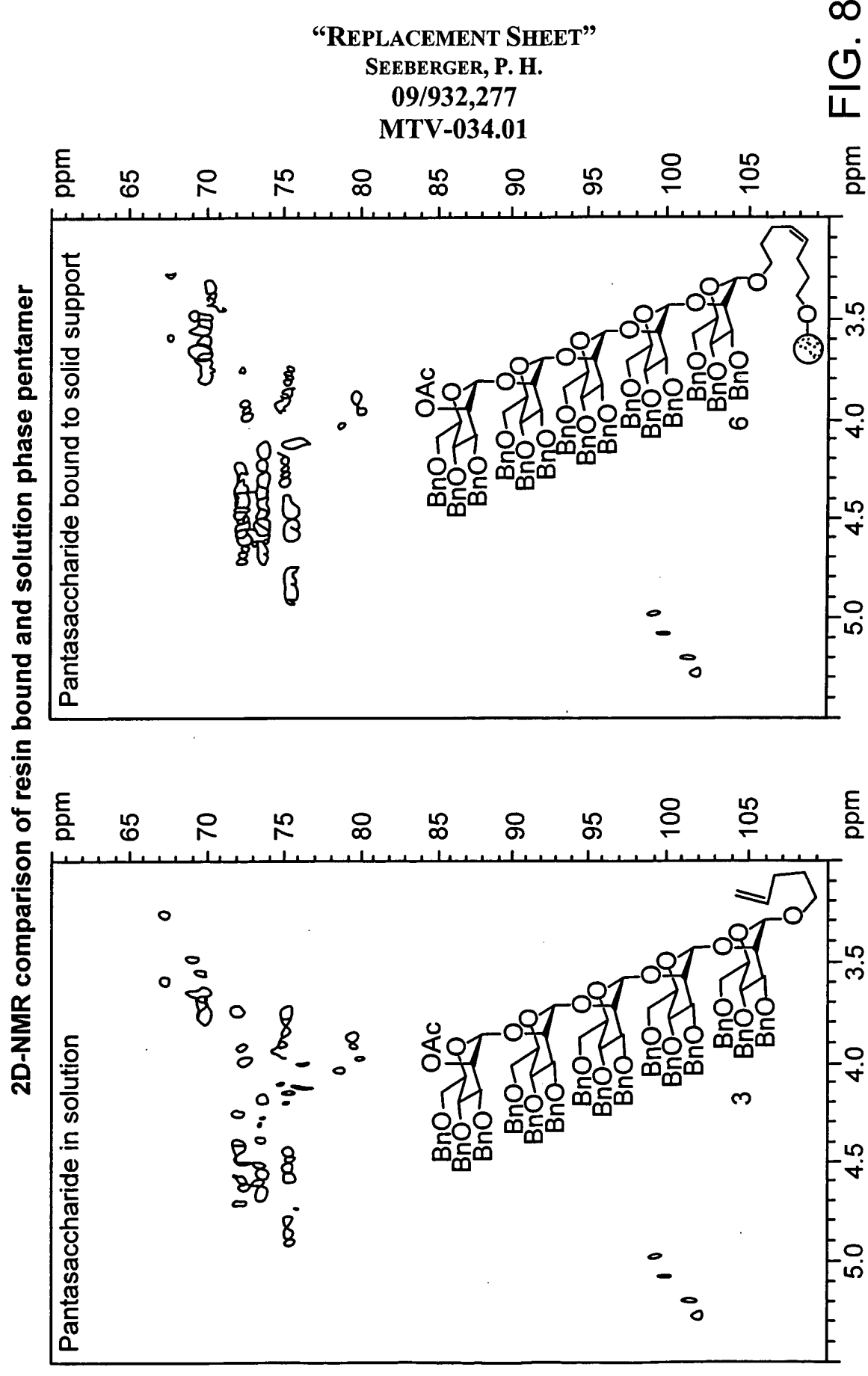
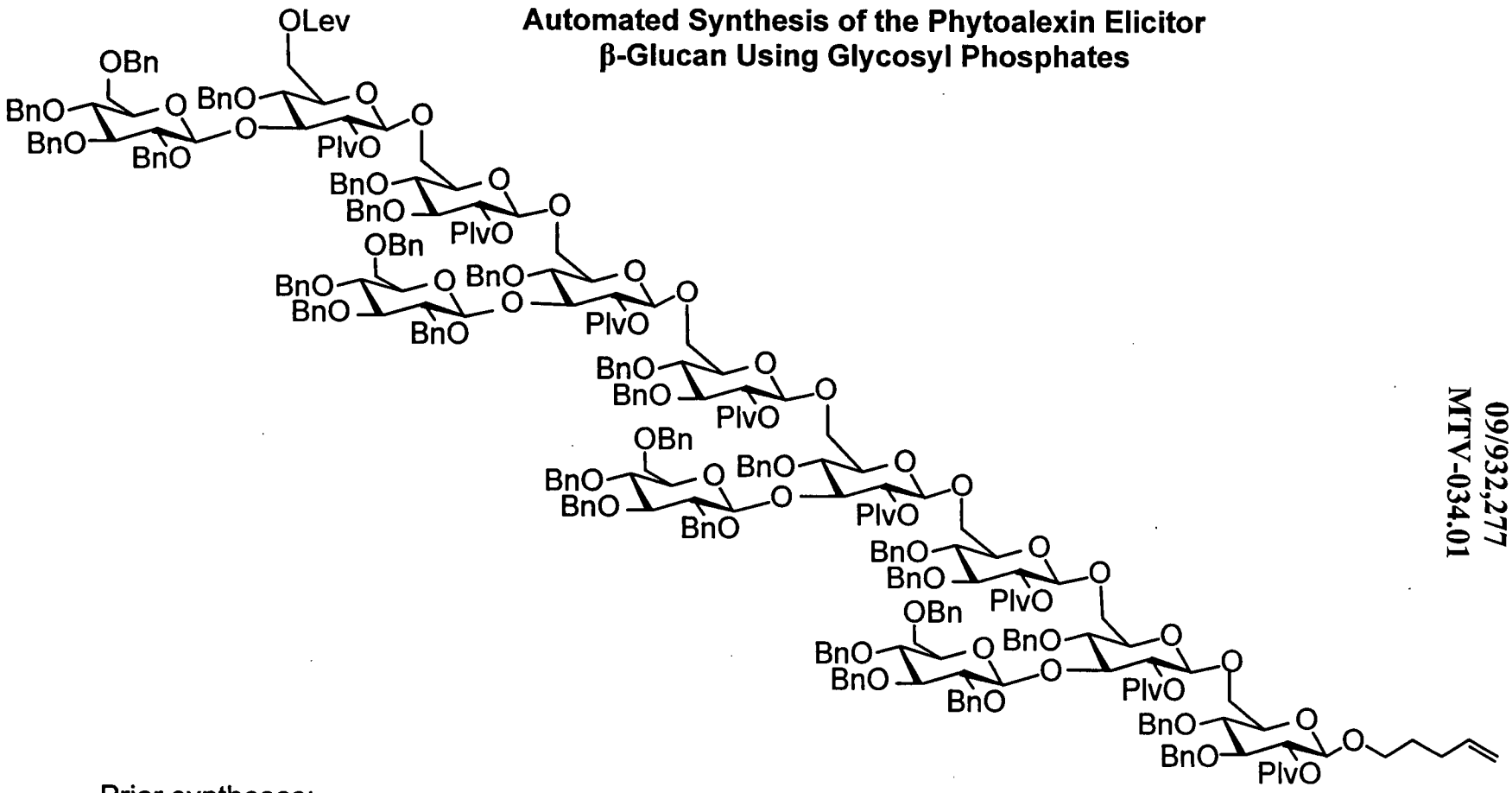


FIG. 8

Automated Synthesis of the Phytoalexin Elicitor β-Glucan Using Glycosyl Phosphates

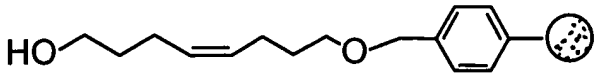


Prior syntheses:
Garegg et al. *Angew. Chem. Int. Ed.* 1983, *22*, 793;
van Boom et al. *Chem. Eur. J.* 1995, *1*, 16;
on soluble support: van Boom et al. *Recl. Trav. Chim. Pays-Bas* 1993; *112*, 464;
on polymer support using trisaccharide blocks: Nicolaou et al. *Angew. Chem. Int. Ed.* 1998, *37*, 1559.

FIG. 9

Automated Oligosaccharide Synthesis

Chemical Issues:

- Choice of Resin (Merrifield's, Argopore, Tentagel)
- Linker: 

- Glycosylation Protocol
- Deprotection Protocol
- Capping Cycle
- Cleavage Method
- Purification Technique

Practical Issues:

- Scale (μmol-mmol)
- Cycle Development/Time
- Temperature Control Device

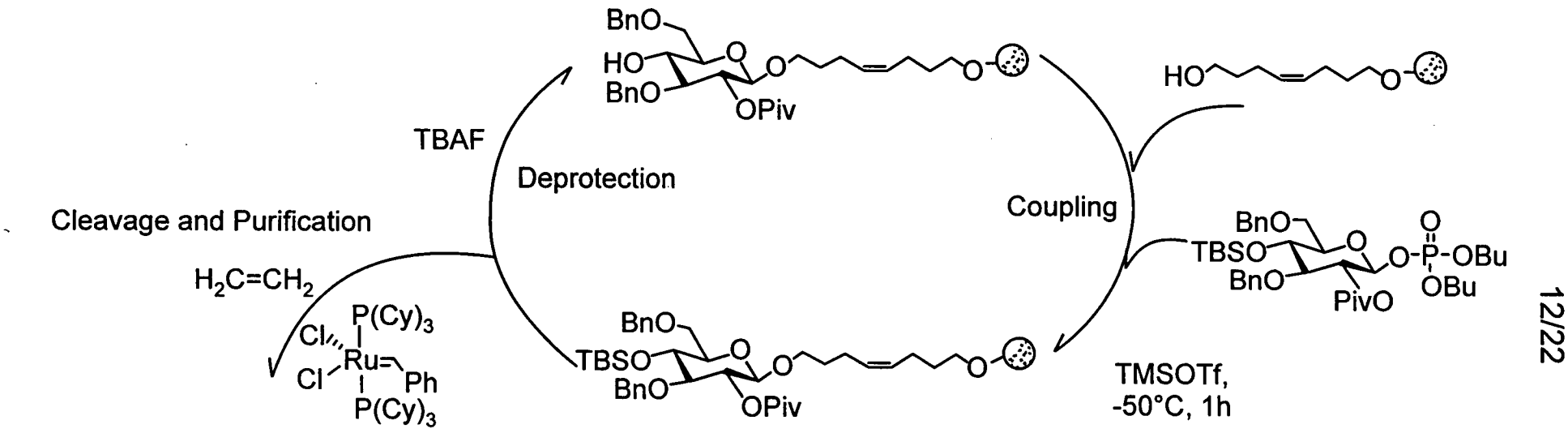
FIG. 10

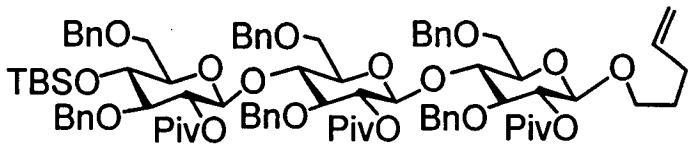
Automated Oligosaccharide Synthesis with Glycosyl Phosphates: Coupling Cycle

	Reagent/Solvent	Equivalents	Temperature	Time
Coupling	Donor	5	-15°C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			5 min
	THF			
Coupling	Donor	5	-15°C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			5 min
	THF			
Deprotection	N_2H_4-HOAc		15°C	30 min
Washing	Pyr./AcOH			5 min
Deprotection	N_2H_4-HOAc		15°C	30 min
Washing	Pyr./AcOH			5 min
		Cycle Time per residue		110 min

FIG. 11

Solid Support Oligosaccharide Synthesis:
Glycosyl Phosphate Donors





53% overall yield

Advantages:
- excess reagents drive reactions to completion
- purification only at the end of the synthesis

FIG. 12

Automated Hexasaccharide Synthesis Using Glycosyl Phosphates

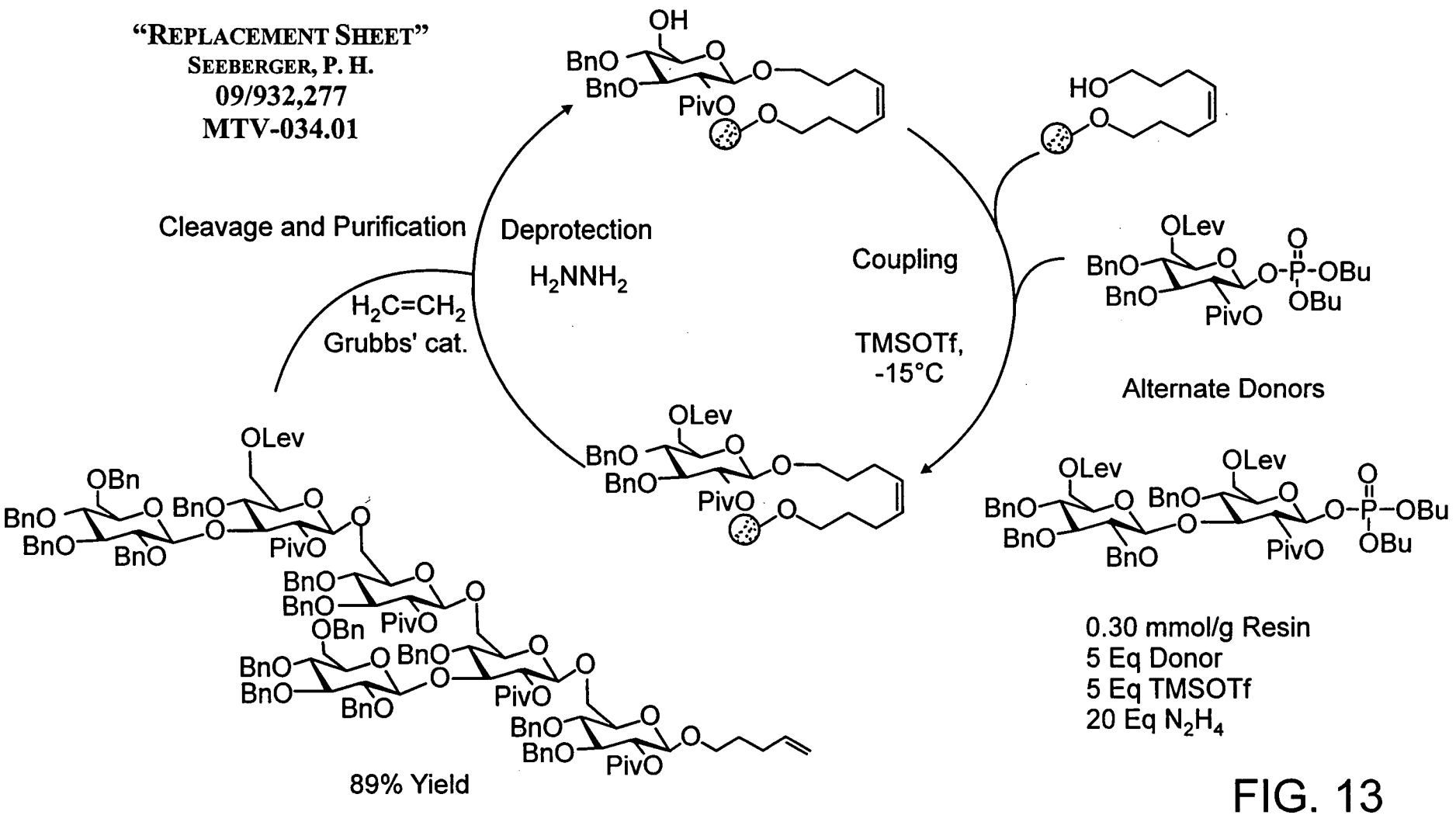


FIG. 13

Crude HPLC Profile of the Hexamer Synthesis

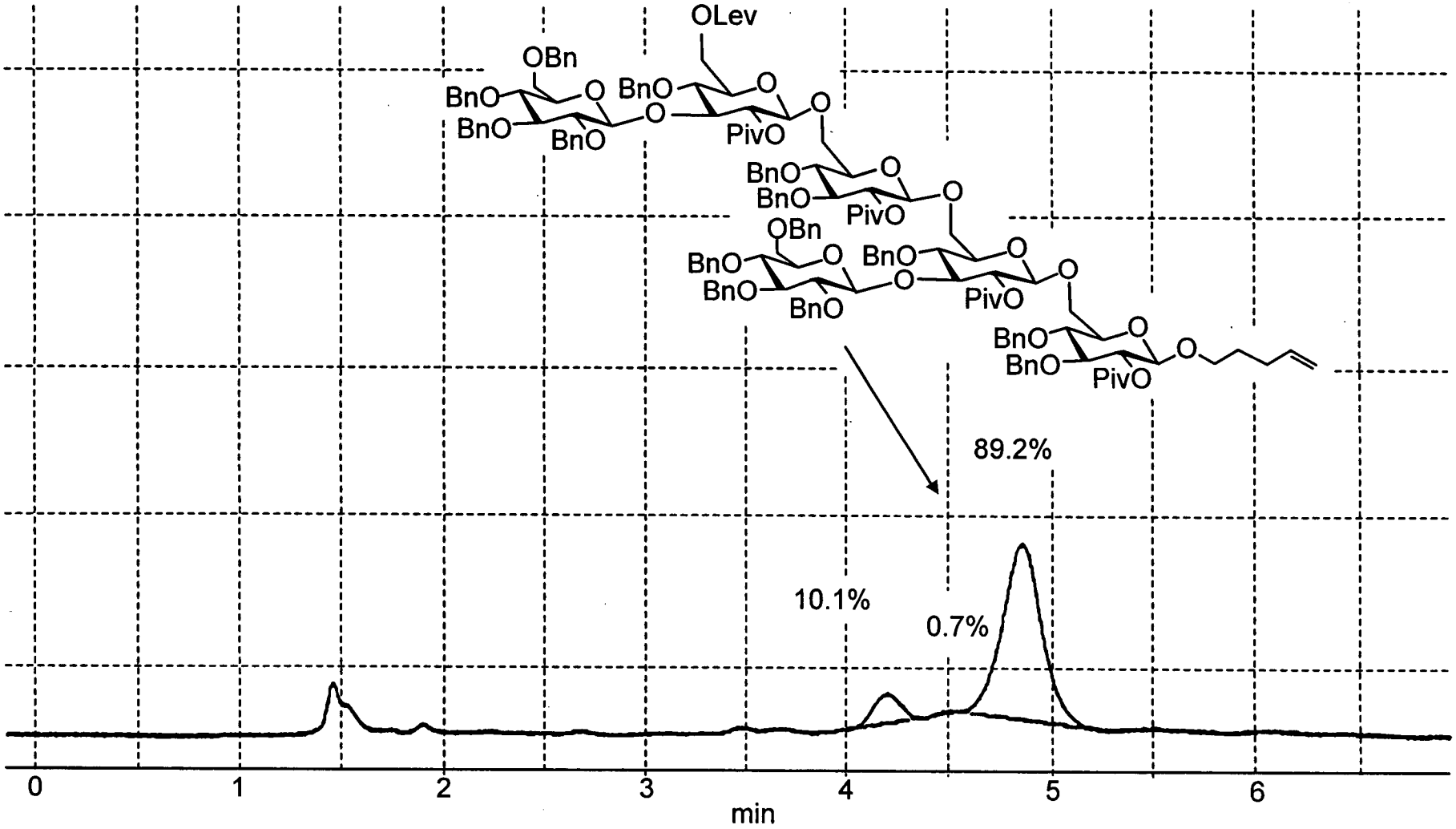


FIG. 14

Automated Oligomannoside Synthesis: Coupling Cycles

	Reagent/Solvent	Equivalents	Time
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
25μmol Scale	Cycle Time per residue		140 min

FIG. 15

Solid-Phase Oligosaccharide Synthesis:
Coupling Cycle Development

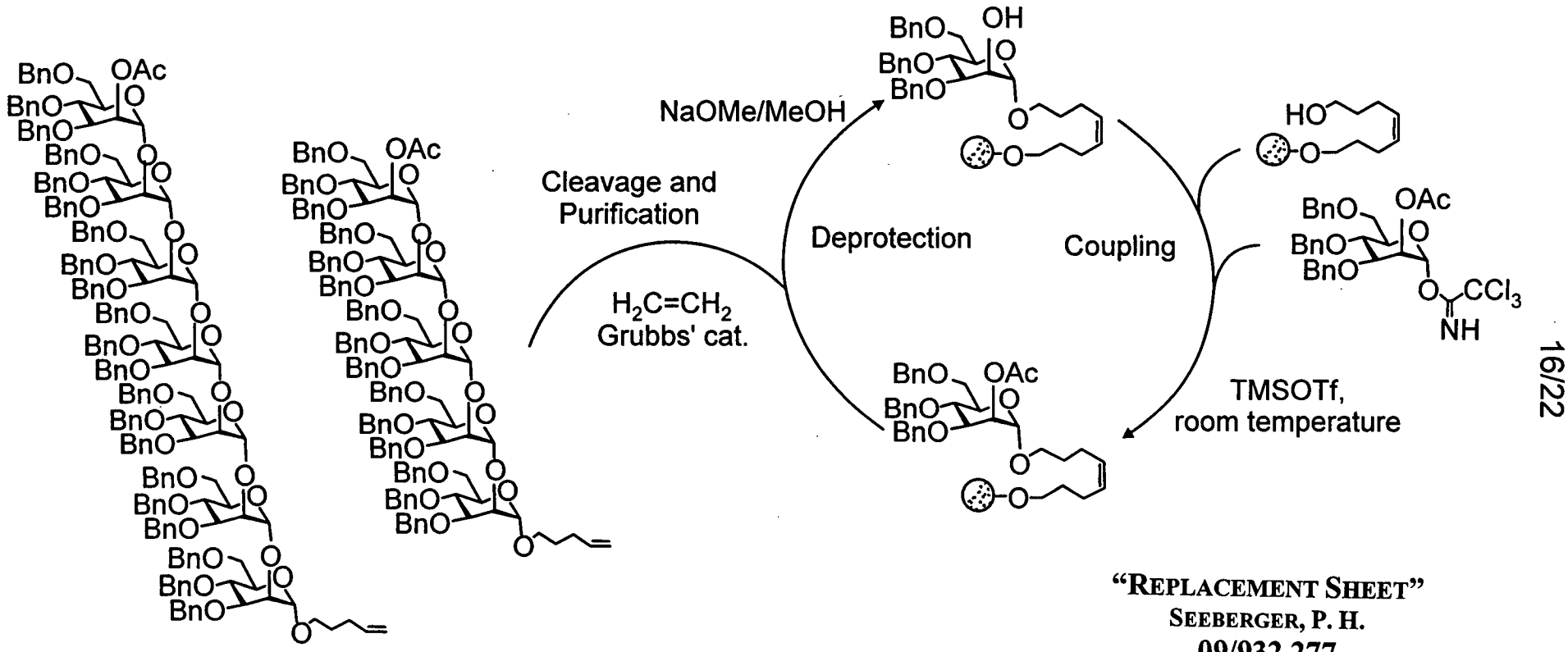


FIG. 16

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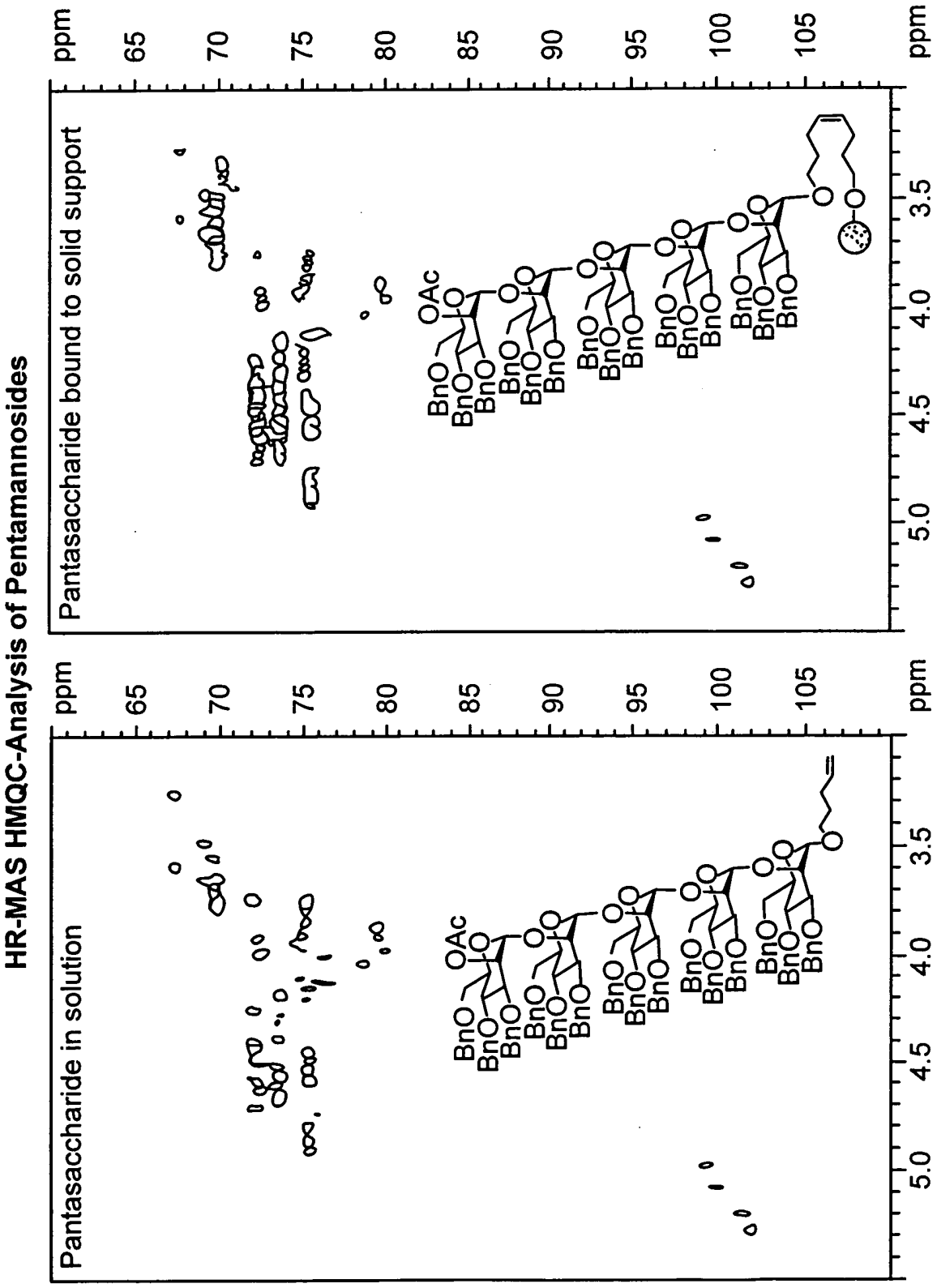

FIG. 17

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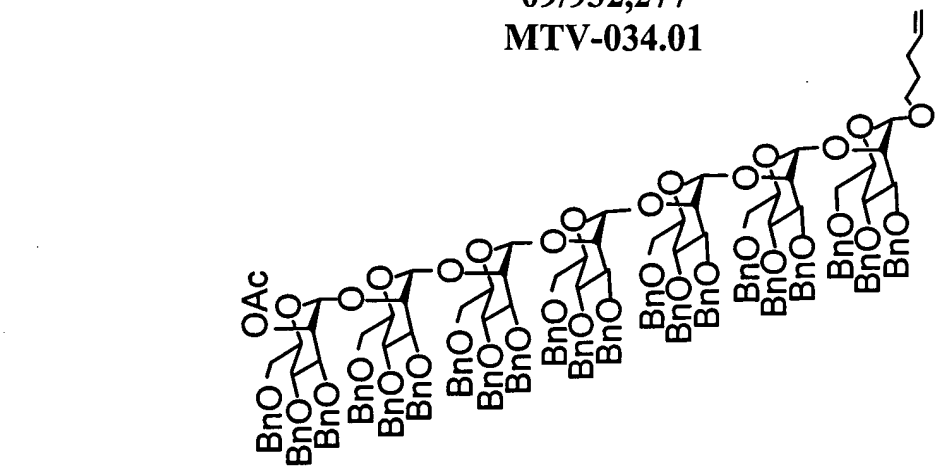

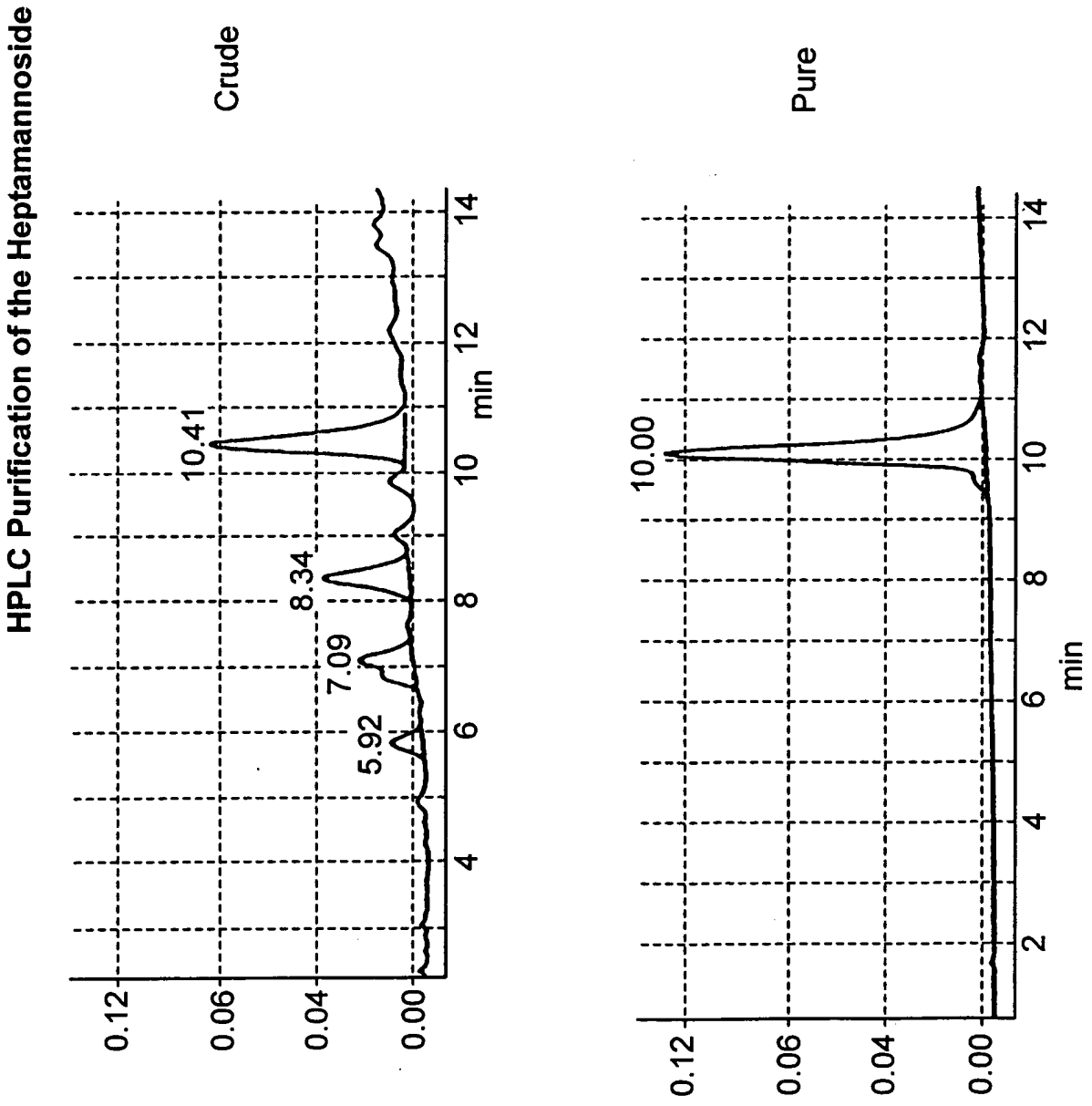

FIG. 18

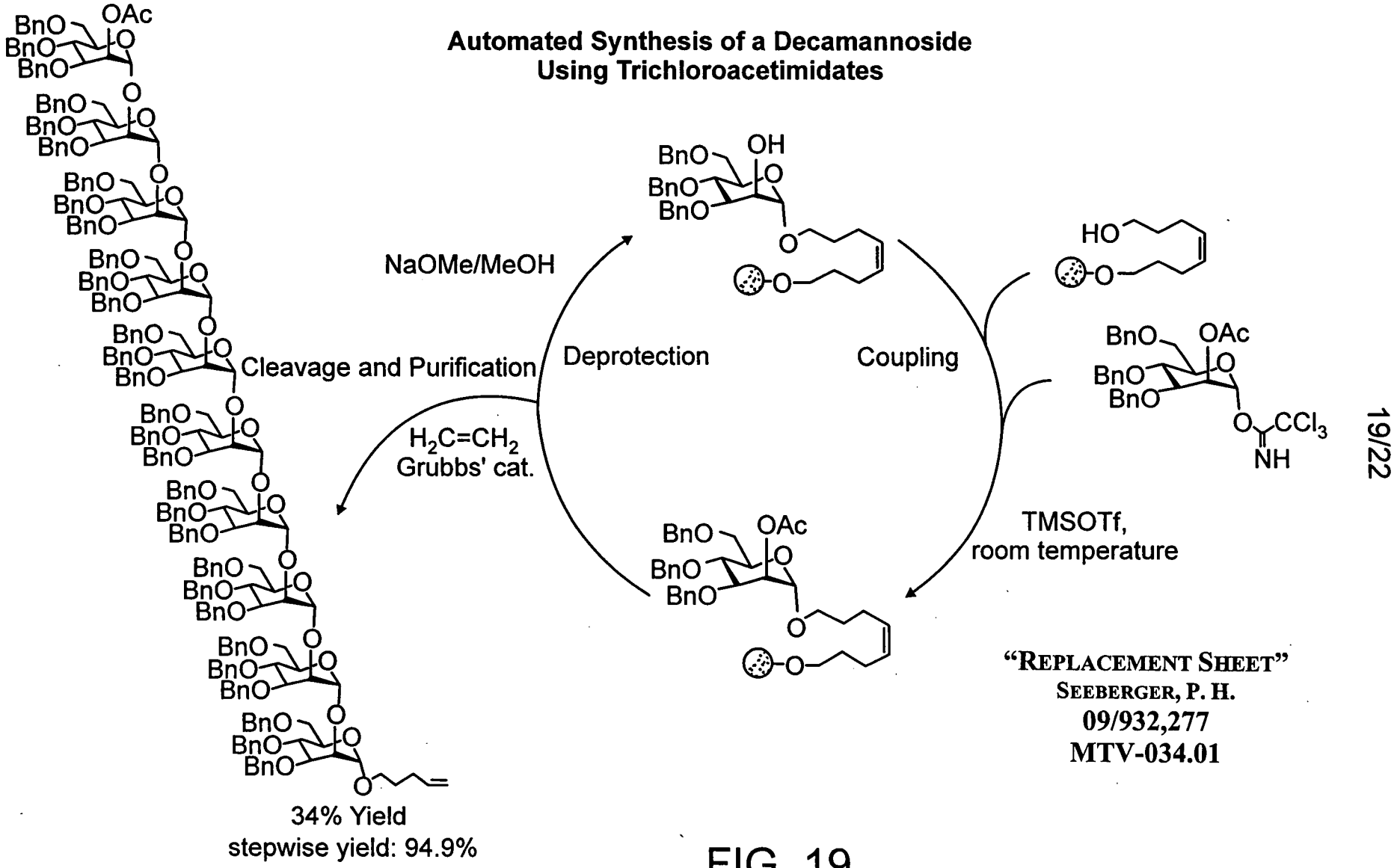

FIG. 19

Automated Synthesis of Leishmania Cap Tetrasaccharide

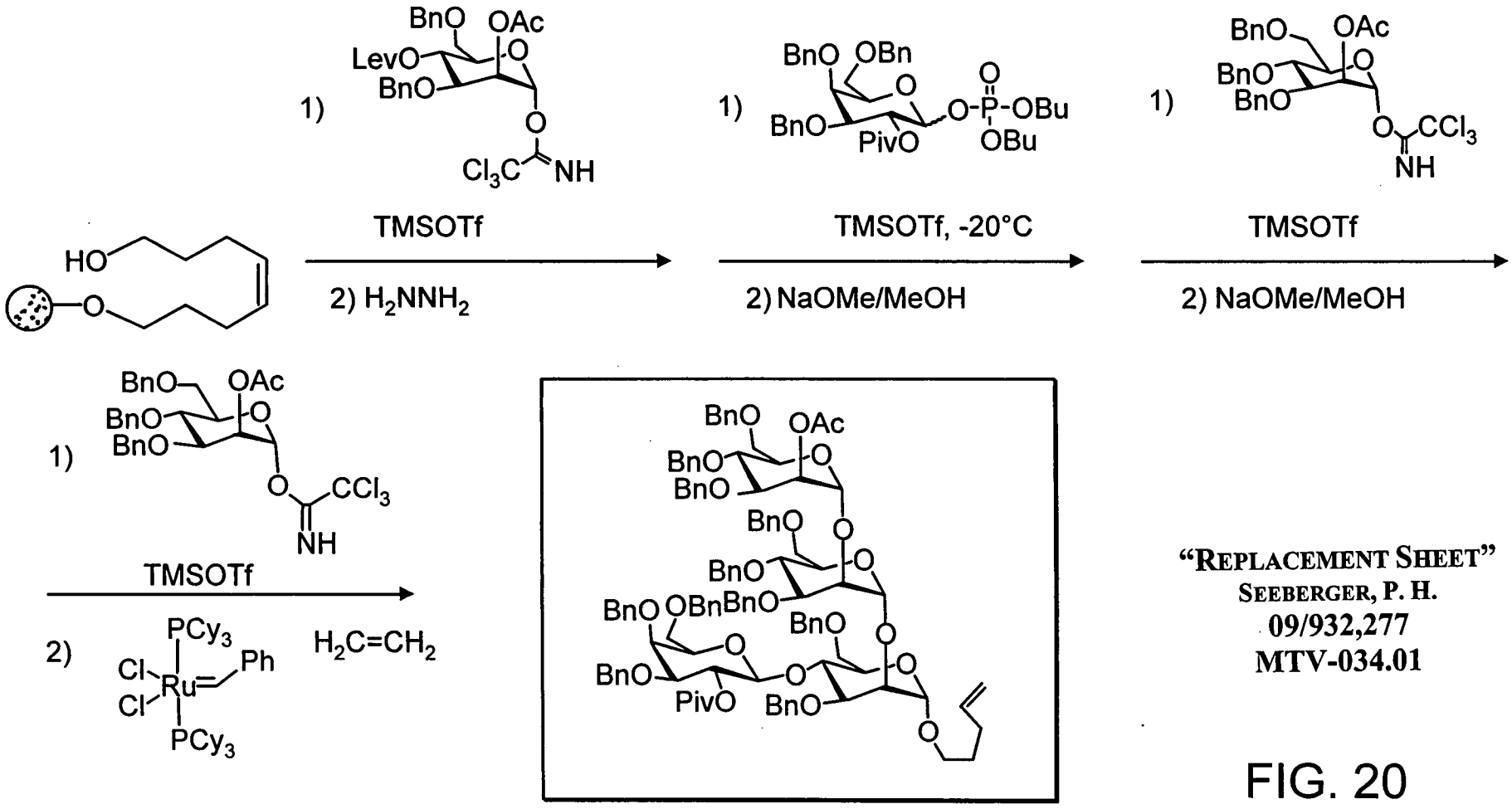

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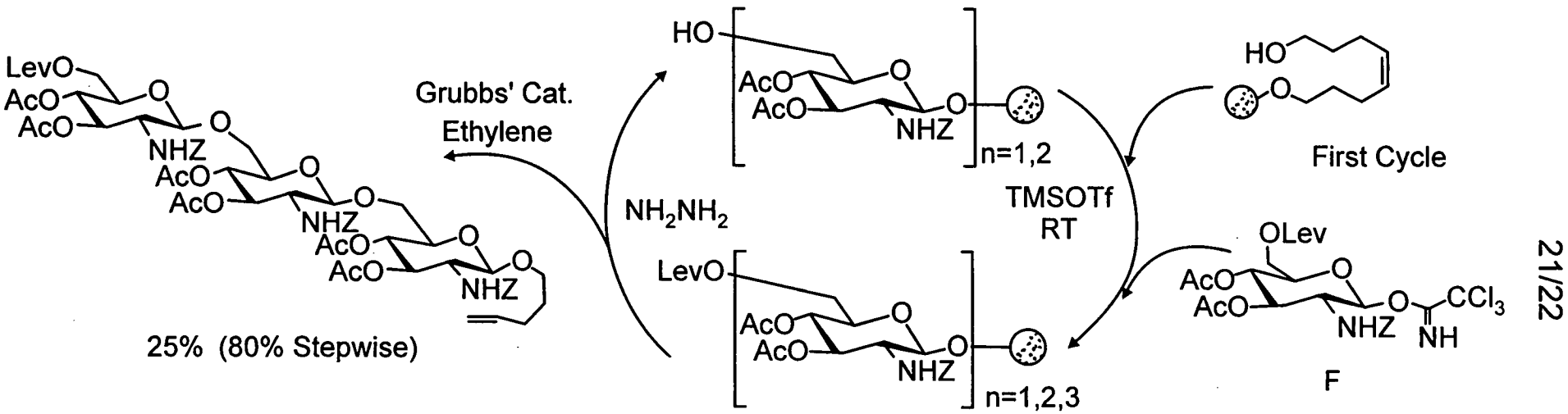
FIG. 20

Automated Synthesis of GlcA Trisaccharide



Cycle:

Time: 8.5h
Donor: 5.0 eq
Activator: 0.5eq TMSOTf
Deprotection: 0.5 M $NH_2NH_2 \bullet H_2O$

FIG. 21

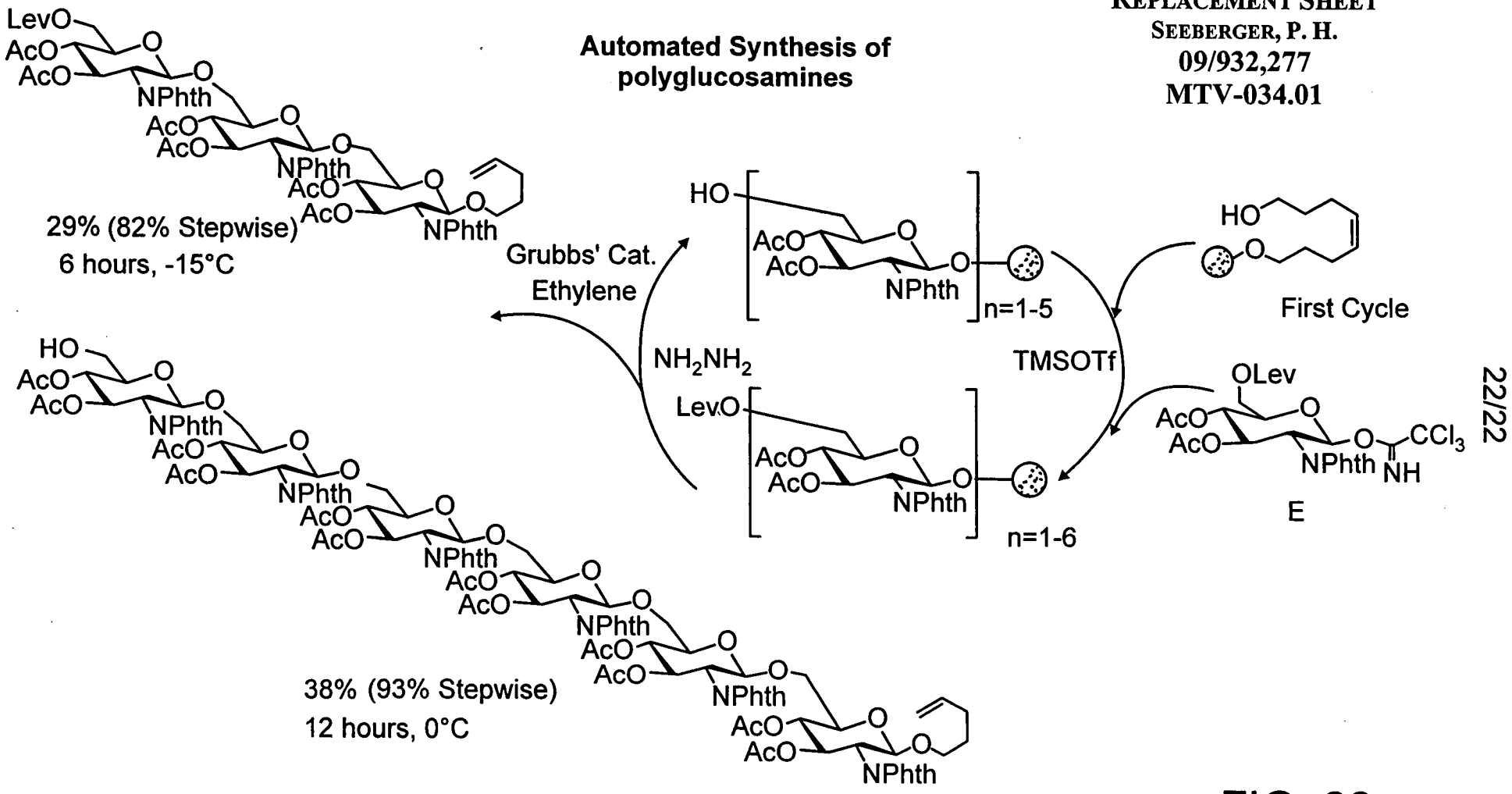

Automated Synthesis of polyglucosamines
29% (82% Stepwise)
6 hours, -15°C
Grubbs' Cat.
Ethylene
NH_2NH_2
TMSOTf
First Cycle
n=1-5
n=1-6
E
38% (93% Stepwise)
12 hours, 0°C

FIG. 22